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L1: Entry 37 of 76 File: USPT Aug 22, 2000

DOCUMENT-IDENTIFIER: US 6107090 A
TITLE: Treatment and diagnosis of prostate cancer with antibodies to extracellur PSMA domains

Other Reference Publication (14):
Chang et al., "Five Different Anti-Prostate-specific Membrane Antigen (PSMA) Antibodies Confirm PSMA Expression in Tumor-associated Neovasculature," Cancer Res., 59:3192-3198 (1999).

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L1: Entry 62 of 76 File: USPT Dec 26, 1995

DOCUMENT-IDENTIFIER: US 5478556 A
TITLE: Vaccination of cancer patients using tumor-associated antigens mixed with interleukin-2 and granulocyte-macrophage colony stimulating factor

Detailed Description Paragraph Right (2):
The "Vaccine" is usually customized for an individual patient; that is, the autologous or allogeneic TAA is mixed with one million colony forming units of GM-CFS and with ten thousand IUs of IL-2 (see FIG. 2 for details of the formulation of the vaccine). A number of other commercially available cancer antigens can also be used in the "Vaccine" in addition to TAA, including carcinoembryonic antigen (CEA), CA 15-3, CA 125, CA 19-9 and prostrate specific antigen (PSA). The use of these cancer antigens may be used in concert with autologous or allogeneic TAA.

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L1: Entry 65 of 76 File: USPT Sep 7, 1993

DOCUMENT-IDENTIFIER: US 5242802 A
TITLE: Processes for the stabilization of prostate specific antigen in natural matrices

Brief Summary Paragraph Right (2):
Prostate specific antigen (PSA), a well characterized tumor associated antigen, is a significant diagnostic and prognostic marker in human prostatic carcinoma. As prostate tumor cells release PSA into the bloodstream, PSA concentrations in serum and other body fluids correlate with the progression of primary or metastatic carcinoma. Accordingly, the quantitation of PSA in patient specimens provides clinicians with an effective means of monitoring a therapeutic regimen and evaluating remission or progression of the disease state.

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L1: Entry 76 of 76 File: DWPI Mar 14, 1985

DERWENT-ACC-NO: 1985-074473
DERWENT-WEEK: 199736

TITLE: Complex of therapeutic agent with binding antibody - to extend serum half-life esp. of antiviral interferon without activity loss

Basic Abstract Text (2):
The antibody may be monoclonal or a population of polyclonal antibodies. It may comprise a Fab, Fab' or Fab'2 fragment. The antibody may be hybrid monoclonal with a dual specificity, one against (II) and the other against a disease-associated antigen. Typically one specificity is directed against a tumour associated antigen and the other against an antitumour agent. The antigen is esp. CFA, PAP, PSA or ferritin, while the agent is an interferon.

Equivalent Abstract Text (2):
The antibody may be monoclonal or a population of polyclonal antibodies. It may comprise a Fab, Fab' or Fab'2 fragment. The antibody may be hybrid monoclonal with a dual specificity, one against (II) and the other against a disease-associated antigen. Typically one specificity is directed against a tumour associated antigen and the other against an antitumour agent. The antigen is esp. CFA, PAP, PSA or ferritin, while the agent is an interferon.

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L2: Entry 1 of 24 File: PGPB May 23, 2002

DOCUMENT-IDENTIFIER: US 20020061310 A1
TITLE: Compositions and methods for dendritic cell-based immunotherapy

Detail Description Paragraph (36):
[0063] For example, "tumor-specific antigens" and "tumor-associated antigens" that are characteristic of a particular tissue type, including particular tumor tissues find utility in the immunostimulatory fusion proteins of the invention. Exemplary tumor antigens include, but are not limited to HER-2/neu; prostatic acid phosphate (PAP); MART-1 (associated with melanoma; Coulie, et al., J. Exp. Med. 180:35, 1994; Hawakami, et al., PNAS 91:3515, 1994; Bakker, et al., J. Exp. Med. 179:1005, 1994); the tumor rejection antigen precursors, MAGE, BAGE and GAGE; NY-ESO (cloned from an esophageal cancer); SART-3 (a squamous cell carcinoma antigen), immunoglobulin antigens specific to particular B-cell lymphomas, tumor-associated antigens such as carcinoembryonic antigen (CEA), p53, c-myc, neural cell adhesion molecule (N-CAM) and polymorphic epithelial mucin (PEM), in addition to any of a number of proteins expressed on tumor cells.

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L2: Entry 19 of 24 File: USPT Oct 13, 1987

DOCUMENT-IDENTIFIER: US 4699880 A
TITLE: Method of producing monoclonal anti-idiotype antibody

Brief Summary Paragraph Right (59):
It will be appreciated that the foregoing illustration can be modified further to substitute for the anti-CEA specific antibody and antibody, preferably a monoclonal antibody, which specifically binds another tumor-associated antigen, e.g., alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), colon-specific antigen-p (CSAp), prostatic acid phosphatase (PAP) and the like. Alternatively, the specific antibody can be an antibody which specifically binds a marker associated with an infectious lesion, e.g., an antibody against a virus, a bacterium or other infectious microorganism, a hormone, an enzyme and the like. The method of the invention can be utilized in any assay wherein the antigen is detected by virtue of its inhibition of the reaction between an antibody and its complementary anti-idiotype antibody. More generally, any competitive immunoassay which detects antigen by virtue of its ability to inhibit the formation of an antigen/antibody complex can be modified to substitute anti-idiotype antibody for the antigen, typically in a form wherein either the a-Id or a-Ag is bound to a solid support, and the other component of the pair is labeled.

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L2: Entry 24 of 24 File: DWPI Mar 14, 1985

DERWENT-ACC-NO: 1985-074473
DERWENT-WEEK: 199736

TITLE: Complex of therapeutic agent with binding antibody - to extend serum half-life esp. of antiviral interferon without activity loss

Basic Abstract Text (2):
The antibody may be monoclonal or a population of polyclonal antibodies. It may comprise a Fab, Fab' or Fab'2 fragment. The antibody may be hybrid monoclonal with a dual specificity, one against (II) and the other against a disease-associated antigen. Typically one specificity is directed against a tumour associated antigen and the other against an antitumour agent. The antigen is esp. CFA, PAP, PSA or ferritin, while the agent is an interferon.

Equivalent Abstract Text (2):
The antibody may be monoclonal or a population of polyclonal antibodies. It may comprise a Fab, Fab' or Fab'2 fragment. The antibody may be hybrid monoclonal with a dual specificity, one against (II) and the other against a disease-associated antigen. Typically one specificity is directed against a tumour associated antigen and the other against an antitumour agent. The antigen is esp. CFA, PAP, PSA or ferritin, while the agent is an interferon.

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PAP.DWPI,EPAB,JPAB,USPT,PGPB.	4729
((TAA OR TUMOR ADJ ASSOCIATED) SAME (PROSTATE) AND (PAP OR PSMA)).USPT,PGPB,JPAB,EPAB,DWPI.	62

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L4	(taa or tumor adj associated) same (prostate adj antigen$)	2	L4
L3	(taa or tumor adj associated) same (prostate)	295	L3
L2	(taa or tumor adj associated) same (pap)	24	L2
L1	(taa or tumor adj associated) same (psa or psma)	76	L1

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L5: Entry 11 of 62 File: USPT May 28, 2002

DOCUMENT-IDENTIFIER: US 6395278 B1
TITLE: Prostate specific fusion protein compositions

Brief Summary Paragraph Right (3):
In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins--prostate specific antigen (PSA) and prostatic acid phosphatase (PAP)--have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

Drawing Description Paragraph Type 1 (379):
SEQ ID NO:397 is the cDNA sequence for PAP.

Detailed Description Paragraph Right (10):
Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, Calif.) according to the manufacturer's instructions (and essentially as described by Schena et al., Proc. Natl. Acad Sci. USA 93:10614-10619, 1996 and Heller et al., Proc. Natl. Acad Sci. USA 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

Detailed Description Paragraph Right (135):
Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

Detailed Description Paragraph Table (4):
TABLE IV Prostate-tumor Specific Clones Sequence SEQ ID NO. Designation Comments 401 22545 previously identified P1000C 402 22547 previously identified P704P 403 22548 known 404 22550 known 405 22551 PSA 406 22552 prostate secretory protein 94 407 22553 novel 408 22558 previously identified P509S 409 22562 glandular kallikrein 410 22565 previously identified P1000C 411 22567 PAP 412 22568 B1006C (breast tumor antigen) 413 22570 novel 414 22571 PSA 415 22572 previously identified P706P 416

22573 novel 417 22574 novel 418 22575 novel 419 22580 novel 420 22581 PAP 421 22582 prostatic secretory protein 94 422 22583 novel 423 22584 prostatic secretory protein 94 424 22585 prostatic secretory protein 94 425 22586 known 426 22587 novel 427 22588 novel 428 22589 PAP 429 22590 known 430 22591 PSA 431 22592 known 432 22593 Previously identified P777P 433 22594 T cell receptor gamma chain 434 22595 Previously identified P705P 435 22596 Previously identified P707P 436 22847 PAP 437 22848 known 438 22849 prostatic secretory protein 57 439 22851 PAP 440 22852 PAP 441 22853 PAP 442 22854 previously identified P509S 443 22855 previously identified P705P 444 22856 previously identified P774P 445 22857 PSA 446 23601 previously identified P777P 447 23602 PSA 448 23605 PSA 449 23606 PSA 450 23612 novel 451 23614 PSA 452 23618 previously identified P1000C 453 23622 previously identified P705P

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L5: Entry 44 of 62 File: USPT Feb 6, 1996

DOCUMENT-IDENTIFIER: US 5489525 A
TITLE: Monoclonal antibodies to prostate cells

Brief Summary Paragraph Right (3):
Among the methods employed for detection of prostate cancer, the digital rectal exam is the oldest and simplest, but in 70% of patients the exam fails to reveal cancer until it has spread to other parts of the body. Because of the high miss rate, such exams are now being used in conjunction with a blood test for prostate specific antigen (PSA), which was first isolated in 1979. PSA is recognized as the best tumor marker presently available, being more sensitive and more specific than either the rectal exam or the prostatic acid phosphatase test. The PSA protein is made and secreted by both normal and cancerous prostate cells, but is elevated in the blood of men with prostate cancer. The older prostatic acid phosphatase (PAP) test has been displaced by the PSA assay, although it remains a tool for monitoring metastases and response to therapy, especially endocrine treatment.

Other Reference Publication (7):
Starling et al., "Disulfide Bonding of a Human Prostate Tumor-associated Membrane Antigen Recognized by Monoclonal Antibody D83.21", Cancer Res. 45:804-808 (Feb., 1985).

Other Reference Publication (11):
Kim et al., "Monoclonal Antibody PR92 with Restricted Specificity for Tumor-associated Antigen of Prostate and Breast Carcinoma", Cancer Res. 48:4543-4548 (Aug. 15, 1988).

Other Reference Publication (18):
Lipford et al., "Comparative Study of Monoclonal Antibodies TURP-27 and HNK-1: Their Relationship to Neural Cell Adhesion Molecules and Prostate Tumor-associated Antigens", Cancer Res. 51: 2296-2301 (May 1, 1991).

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L5: Entry 56 of 62 File: USPT May 7, 1991

DOCUMENT-IDENTIFIER: US 5013645 A
TITLE: Immunological methods and materials for detection of tumor associated antigens

Abstract Paragraph Left (1):
Disclosed are immunological methods and materials for detection of antigens associated with breast or prostate cancer disease states. Presently preferred antibody preparations (e.g., PR92 monoclonal antibodies produced by hybridoma cell line ATCC HB 9390) are employed in immunoassays performed on patient body fluids and for purification of tumor-associated antigen compositions.

Brief Summary Paragraph Right (4):
Of interest to the background of the present invention are the following references relating to the diagnosis of prostate cancer disease states on the basis of elevated levels of marker substances such as "prostate specific antigen" (PA) and prostatic acid phosphatase (PAP) which are present in low levels in normal human serum and the serum of patients with benign prostatic hyperplasia, but present at higher levels in sera of prostatic carcinoma patients, especially those in an advanced disease state: Lin, et al., U.S. Pat. No. 4,298,592; Lee, et al., U.S. Pat. No. 4,267,272; Miller, et al., U.S. Pat. No. 4,510,239; and, European Patent Application No. 160228 published Nov. 6, 1985.

Detailed Description Paragraph Right (1):
The following illustrative examples relate to the development of monoclonal antibodies which specifically react with tumor associated antigens found in body fluids of individuals with breast or prostate cancer. More specifically, Example 1 relates to the procedures whereby hybridoma cell lines secreting monoclonal antibodies were generated. Example 2 relates to characterization of antibodies produced by a selected hybridoma cell line. Example 3 relates to a radio-immunoassay based on a selected monoclonal antibody and use of this radioimmunoassay in screening for reactivity with known tumor-associated markers. Examples 4, 5, 6, 7 and 8 relate to immunoassay techniques applied to the measurement of antigens in fluid samples of prostate and breast cancer patients. Example 9 relates to immunopurification and characterization of PR92 antigen compositions. Example 10 relates to the use of the PR92 Mab radioimmunoassay procedure as an aid in the diagnosis and prognosis of cancer patients. Examples 11, 12 and 13 relate to the production of PR92 antigen from cells and tissue cultures.

Detailed Description Paragraph Right (8):
The hybridoma clones were screened against DU145, human fetal kidney (HFK) cell extracts, CEA and PAP antigens. Sixteen hybridomas exhibiting strong binding with the DU145 cell line and essentially no binding with HFK cell extracts, CEA or PAP were then selected to be grown in vivo. Balb/C females were injected intraperitoneally with 45.times.10.sup.6 hybridoma cells. The ascites fluid suspensions were passed every 7-10 days. Antibodies of the 16 clones were further assayed for binding specificity using tumor cell lines listed in Table I.

Detailed Description Paragraph Right (14):
In order to determine the specificity of the PR92 Mab radioimmunoassay, a number of cancer cell markers were tested. These included the DU145 cell extract and prostatic acid phosphatase (PAP), one of the presently utilized "markers" for prostate cancer. Also included were: prostate specific antigen (PA); carcinoembryonic antigen (CEA); alfa-fetoprotein; ferritin; blood group substances (A, B, H, T); the Centocor

commercial assay antigens CA 19-9, CA 125, and CA 15-3; Human actin; Fibrinogen; Human colonic mucin; Seminal plasma; and .beta.-2 Microglobulin. The results shown in Table III indicate that the radioimmunoassay specifically detects antigens present in the DU145 cell extract.

Detailed Description Paragraph Right (17):
A correlative study of serum samples from normal males and males diagnosed for benign prostate disease or for prostate cancer was performed using the prostatic acid phosphatase (PAP) enzyme immunoassay. Nine of sixty normal male serum samples displayed PAP levels in excess of the baseline level ordinarily delineating "positive" and "negative" results. Similarly elevated PAP levels were detected in two of twenty-eight serum samples from benign prostate disease patients. In contrast to the PR92 Mab assay study, only sixteen of the thirty-one prostate cancer patient serum samples tested as "positive" according to the PAP assay.

Detailed Description Paragraph Right (18):
The above results indicate a higher degree of specificity and sensitivity in prostate cancer detection using the PR92 Mab RIA rather than using the PAP enzyme immunoassay.

Detailed Description Paragraph Right (29):
In one series of experiments, serum samples of five prostate cancer patients were collected over periods ranging from 108 to 719 days, stored at -20.degree. C., and analyzed for PR92 antigen content. The results were correlated to clinical evaluations of the disease state of the patient at the time of sampling. In two instances correlations were also made to results obtained using assays for PAP and PA, commercially available from Abbott Laboratories, North Chicago, Ill. (PAP) and Cetus Corporation, Emeryville, Calif. (PA). The resulting data are set forth in FIGS. 3, 4 and 5.

Detailed Description Paragraph Right (31):
The data set forth in FIGS. 3, 4, and 5 reveal a high degree of correlation between serum PR92 levels and the clinical evaluations. Significantly, no similar correlations could be drawn with respect to the PAP and PA test results.

Detailed Description Paragraph Table (3):
TABLE III _____ Detection of Tumor-associated Markers Using PR92 Mab Radioimmunoassay Highest concentration Marker Detection tested _____ DU145 cell extract + Cell extract Prostatic acid - 30 ng/ml phosphatase Prostate specific - 50 ng/ml antigen Carcinoembryonic - 60 ng/ml antigen Alfa-fetoprotein - 40 ng/ml Ferritin - 400 ng/ml Human blood group - Erythrocyte substance A,B,H,T. extract CA 19-9 - 120 units/mL CA 125 - 500 units/mL CA 15-3 - 200 units/mL Human actin - 50 ug/mL Fibrinogen - 1 ug/mL Human colonic mucin - 1 ug/mL Seminal plasma - 10-fold dilution .beta.-2 Microglobulin - 2 ug/mL _____

CLAIMS:

1. In a method for determining the presence of a prostate or breast cancer disease state in a human patient wherein a patient body fluid sample is subjected to analysis for detection of a tumor-associated antigen, wherein the improvement comprises analyzing said fluid sample for the presence of the tumor-associated antigen, specifically immunoreactive with the monoclonal antibody produced by murine derived hybridoma cell line ATCC HB 9390 and having a molecular weight of about 420,000 to about 520,000 daltons under non-reducing conditions, and thereby determining the presence of a prostate or breast cancer disease state.

9. An assay procedure for the detection of prostate or breast tumor-associated antigens in a fluid sample of a patient, said procedure comprising the steps of:

(a) incubating said fluid sample with a solid support to which monoclonal antibodies produced by hybridoma cell line ATCC HB 9390 have been affixed to form a first reaction mixture comprising said monoclonal antibodies and tumor-associated antigens bound thereto, wherein the tumor-associated antigens have a molecular weight of about 420,000 to about 520,000 daltons under non-reducing conditions;

(b) removing unbound components of said fluid sample from said first reaction mixture;

(c) incubating said first reaction with labeled monoclonal antibodies produced by hybridoma cell line ATCC HB 9390 to form a second reaction mixture;

(d) removing unbound labeled monoclonal antibodies from said second reaction mixture; and

(e) determining the extent to which labeled monoclonal antibodies are bound in said second reaction mixture, thereby detecting prostate or breast tumor-associated antigens in the fluid sample.

10. A kit for detection of prostate or breast tumor-associated antigens having a molecular weight of about 420,000 to about 520,000 daltons under non-reducing conditions, comprising in containers:

(a) a monoclonal antibody produced by hybridoma cell line ATCC HB 9390 bound to a solid support; and

(b) a labeled monoclonal antibody produced by hybridoma cell line ATCC HB 9390.

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PROSTATES.DWPI,EPAB,JPAB,USPT,PGPB.	414
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